REMARKS

In response to Office Action mailed on August 28, 2006, Applicants have amended the claims to delete the term "macular degeneration". The amended claims are drawn to a method of alleviating a symptom of dry eye syndrome by administering to a subject suffering from or at risk of developing dry eye a composition containing a carotenoid and a polyphenol and co-administering to the subject a composition comprising an omega-3 fatty acid.

New claims have been added. New claim 107 is supported by disclosure at page 3, line 2; new claims 108-113 are supported by disclosure throughout the specification, e.g., Tables A and B at pages 14-16. No new matter has been added by this amendment.

35 U.S.C. 103

Claims 68-83 were rejected for obviousness over Gorsek in view of Kamarei. The Examiner states:

> Gorsek teaches the use of a carotenoid in combination with polyphenol, a glutathion precursor, a vitamin antioxidant and a lipoic acid in a pharmaceutical formulation for the treatment of an ophthalmic disorder such as macular degeneration. See abstract, table 1 and claims 1-3. The above reference differs from the claimed invention in the presence of an omega-3 fatty acid. Kammari (sic) et al. teach the claimsed omega-3 fatty acids such as eicosapeaenoic acid and docasahexaenoic acid have been previously used in a pharmaceutical formulation for the treatment of ophthalmic angiogenic disorders. See abstract, figures 6 and 7. It would have been obvious to a person skilled in the art to incorporate EPA and DHA into the primary reference, considering that Kammari (sic) et al. teach the addition of such agents to the ophthalmic formulations for the treatment of ophthalmic angiogenic condtions is old and well known
>
> One skilled in the art would have been motivated to combine the teachings of the above references, since one relates to the use of a carotenoid, a polyphenol, a lipoic acid, a vitamin and a glutathion precursor for the treatment of ophthalmic conditions

such as macular degeneration, which is an angiogenic disorder and the other relates to the use of EPA and DHA for the treatment of ophthalmic angiogenic conditions.

The amended claims are drawn to alleviating a symptom of dry eye syndrome. Dry eye syndrome is a condition in which the amount and composition of tears is altered leading to dryness, pain, redness, and irritation.

The Gorsek reference describes a formulation for treatment of age-related macular degeneration, cataracts, elevated ocular pressure, diabetic neuropathy, and glaucoma. However, Gorsek does not describe or suggest dry eye syndrome. Kamarei et al. also fail to describe or suggest dry eye syndrome, much less indicate that omega-3 fatty acids would be useful to treat such a condition. In fact, the Kamarei reference fails altogether to describe an ophthalmic disorder. Rather it describes a method of provoking or enhancing angiogenesis as demonstrated using two different assays to measure angiogenesis – the chorionic allantoic membrane assay and the rabbit cornea assay. Thus contrary to the Examiner's comments, there is no motivation to combine these two references. Even if they were properly combined, the aggregate description provided by these two references is devoid of any disclosure pertaining dry eye syndrome or alleviation of symptoms thereof.

Inflammation, not angiogenesis, is universally recognized as the primary cause of dry eye (see Declaration of Steven G. Pratt (11/12/05); of record)). In that declaration, Dr. Pratt also presents evidence of the unexpected efficacy of the claimed methods in reducing symptoms of dry eye syndrome. The study comparing an ophthalmic formulation such as Gorsek's with the formulation of the claimed method was carried out

using a rigorous and art-recognized test format, in which subjects were exposed to a controlled adverse environment (CAE). The data indicated that the claimed methods were "significantly and surprisingly more effective than Placebo [multivitamin]" for the alleviation of symptoms of dry eye syndrome. Dr. Pratt provided evidence of "[t]he striking level of reduction of patient discomfort and significant decrease in objective indicia of ocular tissue inflammation". Mr. Ousler who managed the clinical trial stated that administration of an oral formulation according to the claimed methods "provided a remarkable reduction in Dry Eye symptoms during CAE." (Declaration of George Ousler (11/15/05; of record))

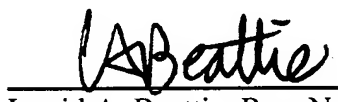
Applicants submit that the claims as now amended are nonobvious over the cited prior art. Further, the data provided in Dr. Pratt's and Mr. Ousler's declaration represent compelling evidence of the surprising results achieved using the claimed methods for alleviating symptoms of dry eye syndrome. Thus, even if a *prima facie* case for obviousness had been established, the foregoing evidence of unexpected results and advantages in a clinical trial is sufficient to overcome the rejection. Withdrawal of this rejection is therefore respectfully requested.

CONCLUSION

Applicants believe that the application and claims are in condition for allowance. The Examiner is invited to contact the undersigned at the number or email listed below should she believe that there are any remaining issues that could be more easily resolved by personal or telephonic interview.

With a three-month extension of time, these documents are due on or before February 28, 2007. Applicants submit herewith a Petition for a Three-Month Extension of Time, along with a check for the fee of $510.00. The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21534-002CIP.

Respectfully submitted,



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Dated: February 28, 2007

TRA 3135077